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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : MARTIN et al.
U.S. Serial No.: 10/518,003
Filed : March 14, 2005
For : IN-VIVO ENERGY DEPLETING STRATEGIES FOR
KILLING DRUG-RESISTANT CANCER CELLS

Law Offices of Albert Wai-Kit Chan, LLC
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October 29, 2007

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

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Sir/Madam:

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

In accordance with their duty of disclosure under 37 C.F.R. §1.56, Applicants would like to direct the Examiner's attention to the following references which are listed below and on forms PTO/SB08A and PTO/SB/08B (which are attached herein as **Exhibit A**) and individual references are further attached as **Exhibits 1-108**.

A copy of the U.S. Patent listed (Reference 1) is on file at the USPTO; therefore, in accordance with 37 C.F.R. 1.98, a copy will not be provided. Applicant's attorney's office may be contacted in the event that the Examiner would like a copy of the reference.

Applicants : MARTIN et al.
U.S. Serial No.: 10/518,003
Filed : March 14, 2005
Examiner : Lawrence E. Crane
Page : 2

Atty. Dkt. No. : 636-C-PCT-US
Art Unit : 1623
Date of SIDS : October 29, 2007

1. U.S. Patent No. 5,641,670, June 24, 1997, TRECO et al.,
"Protein production and protein delivery."
2. International Publication No. WO 02/45720 A1, June 13,
2002 (for Atty. Dkt. #636-A-PCT), SLOAN-KETTERING
INSTITUTE FOR CANCER RESEARCH, "Treatment of cancer by
reduction of intracellular energy and pyrimidines."
[Exhibit 1]
3. PCT International Preliminary Examination Report for
SLOAN KETTERING INSTITUTE FOR CANCER RESEARCH,
PCT/US01/46886 (Atty. Dkt. #636-A-PCT), "Treatment of
cancer by reduction of intracellular energy and
pyrimidines," Filed December 4, 2001, Dated July 25,
2003. [Exhibit 2]
4. Amarante-Mendes, G.P., Finucane, D.M., Martin, S.J.,
Cotter, T.G., Salvesen, G.S. and Green, D.R., 1998,
"Anti-apoptotic oncogenes prevent caspase-dependent and
independent commitment for cell death," Cell Death
Differ., 5:298-306. [Exhibit 3]
5. Batova, A., Diccianni, M.B., Omura, Minamisawa, M., Yu,
J., Carrera, C.J., Bridgeman, L.J., Kung, F.H., Pullen,
J., Amyulong, M.D. and Yu, A.L., 1999, Use of alanosine
as a methyladenosine phosphorylase - selective therapy
for T-cell acute lymphoblastic leukemia in vitro,"
Cancer Res., 59:1492-1497. [Exhibit 4]
6. Berger, N.A., and Berger, S.J., 1986, "Metabolic
consequences of DNA damage: The role of poly (ADP-
ribose) polymerase as mediator of the suicide response,"

Applicants : MARTIN et al.
U.S. Serial No.: 10/518,003
Filed : March 14, 2005
Examiner : Lawrence E. Crane
Page : 3

Atty. Dkt. No. : 636-C-PCT-US
Art Unit : 1623
Date of SIDS : October 29, 2007

In: L. Grossman, A.C. Upton, (eds.) Mechanisms of DNA Damage and Repair, pp. 357-363. New York: Plenum Publishing Corporation. [Exhibit 5]

7. Berns, A., May 2002, "Senescence: A companion in chemotherapy?" Cancer Cell, 309-311. [Exhibit 6]
8. Bertino, J.R., 1990, "Leucovorin rescue revisited: Editorial," J. Clin. Oncol., 8(2):193-195. [Exhibit 7]
9. Bissett, D., Mcleod, H.L., Sheedy, B., Collier, M., Pithavala, Y., Paradiso, L., Pitsiladas, M. and Cassidy, J., 2001, "Phase 1 dose-escalation and pharmacokinetic study of a novel folate analogue A G 2034," Br. J. Cancer, 84:308-312. [Exhibit 8]
10. Bonfoco, E., Krainc, D., Ankarcrona, M., Nicotera, P. and Lipton, S.A., 1995, "Apoptosis and necrosis: two distinct events induced, respectively, by mild and intense insults with N-methyl-D-aspartate or metric oxide/superoxide in cortical cell cultures," Proc. Natl. Acad. Sci. USA, 92:7162-7166. [Exhibit 9]
11. Bose, R., Verheij, M., Haimovitz-Friedman, A., Scotto, K., Kucks, Z. and Kolesnick, R., 1995, "Ceramide synthase mediates daunorubicin-induced apoptosis: an alternative mechanism for generating death signals," Cell, 82:405-411. [Exhibit 10]
12. Boulares, A.H., Yokovlev, A.G., Ivanova, V., Stoica, B.A., Wang, G., Iyer, S. and Smulson, M., 1999, "Role of poly (ADP-ribose) polymerase (PARP) cleavage in

Applicants : MARTIN et al.
U.S. Serial No.: 10/518,003
Filed : March 14, 2005
Examiner : Lawrence E. Crane
Page : 4

Atty. Dkt. No. : 636-C-PCT-US
Art Unit : 1623
Date of SIDS : October 29, 2007

apoptosis. Caspase-3 resistant PARP mutant increases rates of apoptosis in transfected cells," J. Biol. Chem., 274:22932-22940. [Exhibit 11]

13. Britten, C.D., Rowinsky, E.K., Baker, S.D., Weiss, G.R., Smith, L., Staphenson, J., Rothenberg, M., Smetzer, L., Cramer, J., Collins, W., Von Hoff, D.D., and Eckhardt, S.G., 2000, "A Phase 1 and pharmacokinetic study of the mitochondrial-specific chodacyanine dye analog MKT 011," Clin. Cancer Res., 6:42-49. [Exhibit 12]
14. Bronder, J.L. and Moran, R.G., 2002, "Antifolates targeting purine synthesis allow entry of tumor cells into S phase regardless of p53 function," Cancer Res., 62:5236-5241. [Exhibit 13]
15. Budihardjo, II, Walker, D.L., Svingen, P.A., Buckwalter, C.A., Desnoyers, S., Eckdahl, S., Shah, G.M., Poirier, G.G., Reid, J.M., Ames, M.M., and Kaufmann, S.H., 1998, "6-Aminonicotinamide sensitizes human tumor cell lines to cisplatin," Clinical Cancer Research, 4:117-30. [Exhibit 14]
16. Cahill, D.P., Kinzler, K.W., Vogelstein, B. and Lengauer, C., 1999, "Genetic instability and Darwinian selection tumors," Trends in Cell Biology, 57-60. [Exhibit 15]
17. Carson, D.A., Seto, S., Wasson, B., and Carrera, C., 1986, "DNA strand breaks, NAD metabolism, programmed cell death," Exp. Cell. Res., 164:273-281. [Exhibit 16]

Applicants : MARTIN et al.
U.S. Serial No.: 10/518,003
Filed : March 14, 2005
Examiner : Lawrence E. Crane
Page : 5

Atty. Dkt. No. : 636-C-PCT-US
Art Unit : 1623
Date of SIDS : October 29, 2007

18. Chatterjee, S., Hirota, H., Belfi, C.A., Berger, S.J. and Berger, N.A., 1997, "Hypersensitivity to DNA cross-linking agents associated with up-regulation of glucose-regulated stress protein GRP 78," Cancer Res., 57:5112-5116. [Exhibit 17]
19. Chen, Z.H., Zhang, H. and Savarese, T.M., 1996, "Gene deletion chemoselectivity: codeletion of the genes for p16INK4, methylthioadenosine phosphorylase, and the α - and β -interferons in human pancreatic cell carcinoma lines and its implications for chemotherapy," Cancer Res., 56:1083-1090. [Exhibit 18]
20. Constantini, P., Chernyak, B.V., Petronilli, V. and Bernardi, P., 1996, "Modulation of the mitochondrial permeability transition pore by pyridine nucleotides and dithiol oxidation at two separate sites," J. Biol. Chem., 271:6746-6751. [Exhibit 19]
21. Cory, A.H., and Cory, J.G., 1994, "Use of nucleoside Kinase deficient mouse leukemia L1210 cell lines to determine metabolic routes of activation of antitumor nucleoside analogs," Adv. Enzyme Regul., 34:1-12. [Exhibit 20]
22. Cotter, T.G., Lenon, S.V., Glynn, J.G. and Martin, S.J., 1990, "Cell death via apoptosis and its relationship to growth, development and differentiation of both tumor and normal cells," Anticancer Res., 10:1153-1160. [Exhibit 21]

Applicants : MARTIN et al.
U.S. Serial No.: 10/518,003
Filed : March 14, 2005
Examiner : Lawrence E. Crane
Page : 6

Atty. Dkt. No. : 636-C-PCT-US
Art Unit : 1623
Date of SIDS : October 29, 2007

23. Dang, C.V. and Semenza, G.L., 1999, "Oncogenic alterations metabolism," Trends Biochem. Sci., 24:68-92. [Exhibit 22]
24. Dietrich, L.S., Kaplan, L., and Friedland, I.M., 1958, "Pyridine nucleotide metabolism: mechanism of action of the niacin antagonist, 6-aminonicotinamide," J. Biol. Chem. 233:964-968. [Exhibit 23]
25. Droin, N., Beauchemin, M., Solary, E. and Bertrand, R., 2000, "Identification of a caspase-2 isoform that behaves as endogenous inhibitor of the caspase cascade," Cancer Res., 60:7039-7047. [Exhibit 24]
26. Eguchi, Y., Shimizu, S., and Tsujimoto, Y., 1997, "Intracellular ATP levels determine cell fate by apoptosis or necrosis," Cancer Res., 57:1835-1840. [Exhibit 25]
27. Evtodienko, Y.V., Teplova, V.V., Sidosh, S.S., Ichas, F. and Mazal, J.P., 1996, "Microtubule-active drugs suppress the closure of the permeability transition pore in tumor mitochondria," FEBS Lett., 393:86-88. [Exhibit 26]
28. Fitchen, J.H., Riscoe, M.K., Dana, B.W., Lawrence, H.J. and Ferro, A.J., 1986, "Methylthioadenosine phosphorylase deficiency in human leukemias and solid tumors," Cancer Res., 46:5409-5412. [Exhibit 27]
29. Formigli, L., Papucci, L., Tani, A., Schivone, N., Tempestine, A., Orlandini, G.E., Capaccioli, S. and

Applicants : MARTIN et al.
U.S. Serial No.: 10/518,003
Filed : March 14, 2005
Examiner : Lawrence E. Crane
Page : 7

Atty. Dkt. No. : 636-C-PCT-US
Art Unit : 1623
Date of SIDS : October 29, 2007

Orlandini, S.Z., 2000, "Aponecrosis: Morphological and biochemical exploration of a syncretic process of cell death sharing apoptosis and necrosis," J. Cell Physiol. 182:41-49. **[Exhibit 28]**

30. Forrester, H.B, Albright, N., Ling, C.C. and Dewey, W.C., 2000, "Computerized video time-lapse analysis of apoptosis of REC: Myc cells ,X-radiated in different phases of the cell cycle," Radiat. Res., 154:625-639. **[Exhibit 29]**

31. Gaal, J.C., Smith, K.R., and Pearson, C.K., 1987, "Cellular euthanasia mediated by a nuclear enzyme: A central role for nuclear ADP-ribosylation in cellular metabolism," Trends Biochem. Sci., 12:129-130. **[Exhibit 30]**

32. Gewirtz, D.A., 1999, "A critical evaluation of mechanisms of action proposed for the antitumor effects of the anthracycline antibiotics adriamycin and daunorubicin," Biochem. Pharm., 57:727-741. **[Exhibit 31]**

33. Goldin, A., Kendetti, J.M., MacDonald, J.S., Muggia, F., Henney, J. and DeVita, V.T., 1981, "Current results of the screening program at the Division of Cancer Treatment, National Cancer Institute," Eur. J. Cancer, 17:129. **[Exhibit 32]**

34. Green, D.R., 1998, "Apoptotic pathways: The roads to ruin," Cell, 94:695-698. **[Exhibit 33]**

35. Grindey, G.B., Lowe, J.K., Divekey, A.Y., and Halaka, M.T., 1976, "Potentiation by guanine nucleosides of the

Applicants : MARTIN et al.
U.S. Serial No.: 10/518,003
Filed : March 14, 2005
Examiner : Lawrence E. Crane
Page : 8

Atty. Dkt. No. : 636-C-PCT-US
Art Unit : 1623
Date of SIDS : October 29, 2007

growth-inhibitory effects of adenosine analogues on L1210 and Sarcoma 180 cells in culture," Cancer Res., 36:379-383. **[Exhibit 34]**

36. Haimovitz-Friedman, A., Kan, C.C., Ehleiter, D., Persaud, R.S., McLoughlin, M., Fuks, Z. and Kolesnick, R.N., 1994, "Ionizing radiation acts on cellular membranes to generate ceramide and initiate apoptosis," J.Exp. Med., 180:525-535. **[Exhibit 35]**
37. Herceg, Z. and Wang, Z.Q., 1999, "Failure of poly (ADP/ribose) polymerase cleavage by caspases leads to induction of necrosis and enhanced apoptosis," Mol. Cell Biol., 19:5124-5133. **[Exhibit 36]**
38. Herken, H., Lange, K. and Kolbe, H., 1969, "Brain disorder induced by pharmacological blockage of the pentose phosphate pathway," Biochem. Biophys. Res. Commun., 36:93-100. **[Exhibit 37]**
39. Herter, F., Weissman, S.G., Thompson, H.G. et al., 1961, "Clinical experience with 6-aminonicotinamide," Cancer Res. 21:31-37. **[Exhibit 38]**
40. Hickman, J.A., 1992, "Apoptosis induced by anticancer drugs," Cancer Metast. Rev., 11:121-139. **[Exhibit 39]**
41. Hunting, D., Gowans, B., and Henderson, J.F., 1985, "Effect of 6-AN on cell growth, poly (ADP-ribose) synthesis and nucleotide metabolism," Biochem. Pharmacol., 34:3999-4003. **[Exhibit 40]**

Applicants : MARTIN et al.
U.S. Serial No.: 10/518,003
Filed : March 14, 2005
Examiner : Lawrence E. Crane
Page : 9

Atty. Dkt. No. : 636-C-PCT-US
Art Unit : 1623
Date of SIDS : October 29, 2007

42. Janicke, R.V., Sprengart, M.L., Wati, M.R. and Porter, A.G., 1998, "Caspase-3 is required for DNA fragmentation and morphological changes associated with apoptosis," J. Biol. Chem., 273:9357-9360. **[Exhibit 41]**
43. Janicke, R.U., Ng, P., Sprengart, M.L., and Porter, A.G., 1998, "Caspase-3 is required for alpha-fodrin cleavage but dispensable for cleavage of other death substrates in apoptosis," J. Biol. Chem., 273:15540-5. **[Exhibit 42]**
44. Jones, M., 1980, "Pyrimidine nucleotide biosynthesis in animals: Genes, enzymes and regulation of UMP synthesis," Ann. Rev. Biochem., 49:253-279. **[Exhibit 43]**
45. Kamatani, N., Nelson, Rees, W.A. and Carson, D.A., 1981, "Selective killing of human malignant cell lines deficient in methylthioadenosine phosphorylase, a purine metabolic enzyme," Proc. Natl. Acad. Sci. USA, 78:1219-1223. **[Exhibit 44]**
46. Kass, G.E., Eriksson, J.E., Weis, M., Orrenius, S., and Chow, S.C., 1996, "Chromatin condensation during apoptosis requires ATP," Biochem. J., 318:749-52. **[Exhibit 45]**
47. Kerr, J.F.R., Wyllie, A.H., and Currie, A.R., 1972, "Apoptosis: a basic biological phenomenon with wide-ranging implications in tissue kinetics," Brit. J. Cancer, 26:239-257. **[Exhibit 46]**

Applicants : MARTIN et al.
U.S. Serial No.: 10/518,003
Filed : March 14, 2005
Examiner : Lawrence E. Crane
Page : 10

Atty. Dkt. No. : 636-C-PCT-US
Art Unit : 1623
Date of SIDS : October 29, 2007

48. King, M.P., and Attardi, G., 1989, "Human cells lacking mtDNA: Repopulation with exogenous mitochondria by complementation," Science, 246:500-503. **[Exhibit 47]**
49. King, K.L. and Cidlowski, J.A., 1995, "Cell cycle and apoptosis: Common pathways to life and death," J. Cell Biochem., 58:175-180. **[Exhibit 48]**
50. Ko et al., 2004, "Advanced cancers: eradication in all cases using 3-bromopyruvate therapy to deplete ATP," Biochemical and Biophysical Research Communications, 269-275. **[Exhibit 49]**
51. Kroemer, G., 1997, "Mitochondrial implication in apoptosis. Towards an endosymbiont hypothesis of apoptosis evolution," Cell Death Differ., 4:443-456. **[Exhibit 50]**
52. Kroemer, G., Zamzami, N., and Susin, S.A., 1997, "Mitochondrial control of apoptosis," Immunol. Today, 18:44-51. **[Exhibit 51]**
53. Krug, L.M., Ng, K.K., Kris, M.G., Miller, V.A., Tong, W., Heelan, R.J., Leon, L., Leung, D., Kelly, J., Grant, S.C. and Sirotnak, F.M., 2000, "Phase I and pharmacokinetic study of 10-propargyl-10-deazaaminopterin a new antifolate," Clin. Cancer Res., 3493-3498. **[Exhibit 52]**
54. Kuida, K., Hayder, T.F., Kuan, C.Y., Gu, Y., Taya, C., Karasuyama, H., Su, M.S.S., Radic, P. and Flavell, R.A., 1998, "Reduced apoptosis and cytochrome c- mediated

Applicants : MARTIN et al.
U.S. Serial No.: 10/518,003
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Examiner : Lawrence E. Crane
Page : 11

Atty. Dkt. No. : 636-C-PCT-US
Art Unit : 1623
Date of SIDS : October 29, 2007

caspase activation in mice lacking caspase activation in mice lacking caspase 9," Cell, 94:325-337. **[Exhibit 53]**

55. Lemasters, J.J., 1999, "Necroptosis and the mitochondrial permeability transition: shared pathways to necrosis and apoptosis," Am. J. Physiol., 276:G1-6. **[Exhibit 54]**

56. Li, H., Zhu, H., Xu, C.J., 1998, "Cleavage of BID by caspase 8 mediates the mitochondrial damage in the Fas pathway of apoptosis," Cell, 94:491-501. **[Exhibit 55]**

57. Li, W.W., Cole, P., Martin, D., Banerjee, D. and Bertino, J.R., 2000, "Methylthioadenosine phosphorylase (MTAP) status determines sensitivity to L-alanosine in human soft tissue sarcoma cell lines and is enhanced by 6-methylmercaptopurine riboside (MMPR)," Proc. Am. Assoc. Cancer Res., 41:240. **[Exhibit 56]**

58. Liu, X., Kim, C.N., Yang, J., Jemmerson, R. and Wang, X., 1996, "Induction of apoptotic program in cell-free extracts: requirement for dATP and cytochrome C.," Cell, 86:147-157. **[Exhibit 57]**

59. Lowe, S.W., 1995, "Cancer therapy and p53," Curr. Opin. Oncol., 7:547-553. **[Exhibit 58]**

60. Marks, D.I., and Fox, R.M., 1991, "DNA damage, poly(ADP-ribosyl)ation and apoptotic cell death as a potential common pathway of cytotoxic drug action," Biochem. Pharmacol. 42:1859-1867. **[Exhibit 59]**

Applicants : MARTIN et al.
U.S. Serial No.: 10/518,003
Filed : March 14, 2005
Examiner : Lawrence E. Crane
Page : 12

Atty. Dkt. No. : 636-C-PCT-US
Art Unit : 1623
Date of SIDS : October 29, 2007

61. Martin, D.S., Fugman, R.A., Stolfi, R.L. and Hayworth, E., 1975, "Solid tumor animal model therapeutically predictive for human breast cancer," Cancer Chemother. Rep. Part 2, 5:89. **[Exhibit 60]**
62. Martin, D.S., Stolfi, R.L., and Colofiore, J.R., 1997, "Perspective: The chemotherapeutic relevance of apoptosis and a proposed biochemical cascade for chemotherapeutically-induced apoptosis," Cancer Invest., 15:372-381. **[Exhibit 61]**
63. Martin, D., Matei, C., and Koutcher, J., 2000, "Marked enhancement of radiotherapy-induced tumor regression by an NAD antagonist, 6-aminonicotinamide (6-AN)," Proc. Am. Assoc. Cancer Res., 41:283 (Abstract 1800). **[Exhibit 62]**
64. Modica Napolitano, J.S. and Aprille, J.R., 2001, "Delocalized lipophilic cations selectively target the mitochondria of carcinoma cells," Adv. Drug Deliv. Rev., 49:63-701. **[Exhibit 63]**
65. National Institute of Health Consensus Development Conference Statement, 2001, "Adjuvant Therapy for Breast Cancer, November 1-3, 2000," J. Natl. Cancer Inst., 93:979-989. **[Exhibit 64]**
66. Nguyen, B.T., El Sayed, Y.M., and Sadee, W., 1984, "Interaction among the distinct effects of adenine and guanine depletion in mouse lymphoma cells," Cancer Res., 44:2272-2277. **[Exhibit 65]**

Applicants : MARTIN et al.
U.S. Serial No.: 10/518,003
Filed : March 14, 2005
Examiner : Lawrence E. Crane
Page : 13

Atty. Dkt. No. : 636-C-PCT-US
Art Unit : 1623
Date of SIDS : October 29, 2007

67. Nicotera, P. and Leist, M., 1997, "Mitochondrial signals and energy requirement in cell death," Cell Death Differ, 4:516. [Exhibit 66]
68. Nobori, T., Karras, J.G., Della Razione, F., Waltz, T.Z., Chen P.P. and Carson, D.A., 1991, "Absence of methylthioadenosine phosphorylase in human gliomas," Cancer Res., 51:3193-3197. [Exhibit 67]
69. Nobori, T., Szinai, I., Amox, D., Parker, B., Olopade, O.I., Buchhagen, D.L. and Carson, D.A., 1993, "Methylthioadenosine phosphorylase deficiency in human non-small cell lung cancers," Cancer Res., 53:1098-1101. [Exhibit 68]
70. Presta, M., Rusunati, M., Belleri, M., Morbedelli, L., Ziche, M. and Ribatti, D., 1999, "Purine analogue 6-methylmercaptapurine riboside inhibits early and late phases of the angiogenesis process," Cancer Res., 59:2417-2424. [Exhibit 69]
71. Raffray, M. and Cohen, G.M., 1997, "Apoptosis and necrosis in toxicology: a continuum or distinct modes of cell death?" Pharmacol. Ther., 75:153-177. [Exhibit 70]
72. Reed, J.C., 1995, "Regulation of apoptosis by bcl-2 family proteins and its role in cancer and drug resistance," Curr. Opin. Oncol., 7:541-546. [Exhibit 71]
73. Roy, N., Dveraux, Q.L., Takahashi, R., Salvesen, G.S. and Reed, J.C., 1997, "The c-IAP-1 and c-IAP-2 proteins

Applicants : MARTIN et al.
U.S. Serial No.: 10/518,003
Filed : March 14, 2005
Examiner : Lawrence E. Crane
Page : 14

Atty. Dkt. No. : 636-C-PCT-US
Art Unit : 1623
Date of SIDS : October 29, 2007

are direct inhibitors of specific caspases," EMBO J.,
16:6914-6925. [Exhibit 72]

74. Sausville, E.A. and Feigal, E., 1999, "Evolving approaches to cancer drug discovery and development at the National Cancer Institute," USA Ann. Oncol., 10:1287-1291. [Exhibit 73]
75. Schmitt, C.A. and Lowe, S.W., 2002, "A senescence program controlled by p53 and p16 ink4a contributed to the outcome of cancer therapy," Cell, 109:335-346. [Exhibit 74]
76. Schmitt, C.A. and Lowe, S.W., 2002, "Apoptosis and chemoresistance in transgenic cancer models," J. Mol. Med., 80:137-146. [Exhibit 75]
77. Schraufstatter, I.U., Hinshaw, D.B., Hyslop, P.S., Spragg, R.H., and Cochrane, C.G., 1986, "Oxidant injury of cells DNA strand-breaks activate polyadenosine diphosphate polymerase and lead to depletion of nicotinamide adenine dinucleotide," J. Clin. Invest., 77:1312-1320. [Exhibit 76]
78. Scudiero, D.A., Monks, A., and Sausville, E.A., 1998, "Cell line designation change: Multidrug-resistant cell line in the NCI anticancer screen," J. Natl. Cancer Inst., 90:862. [Exhibit 77]
79. Serafino, A., Sinibaldi-Vallebono, P., Lazzarino, G., Tavazzi, B., DiPierro, D., Rosi, G. and Ravagnan, G., 2000, "Modifications of mitochondria in human tumor

Applicants : MARTIN et al.
U.S. Serial No.: 10/518,003
Filed : March 14, 2005
Examiner : Lawrence E. Crane
Page : 15

Atty. Dkt. No. : 636-C-PCT-US
Art Unit : 1623
Date of SIDS : October 29, 2007

cells during anthracycline-induced apoptosis,"
Anticancer Res., 20:3383-3394. [Exhibit 78]

80. Shantz, G.D., Smith, C.M., Fontanella, L.J., Lau, H.K.F., and Henderson, J.F., 1973, "Inhibition of purine nucleotide metabolism by 6-methylmercaptapurine ribonucleoside and structurally related compounds," Cancer Res., 33:2867-2871. [Exhibit 79]
81. Shimizu, S., Equchi, Y., Kamike, W., Itoh, Y., Hasegawa, J., Yamabe, K., Otsuid, Y., Matsuda, H. and Tsujimoto, Y., 1996, "Induction of apoptosis as well as necrosis by hypoxia and predominant prevention of apoptosis by bcl-2 and bcl-x," Cancer Res., 56:2161-2166. [Exhibit 80]
82. Sirotnak, F.M., De Graw, J.I., Colwell, W.T. and Piper, J.R., 1998, "A new analogue of 10-deazaaminopterin with markedly enhanced curative effects against human tumor xenografts in mice," Cancer Chemother. Pharmacol., 42:313-318. [Exhibit 81]
83. Staunton, M.J. and Gaffney, E.F., 1998, "Apoptosis: basic concepts and potential significance in human cancer," Arch. Pathol. Lab. Med., 122:310-319. [Exhibit 82]
84. Stolfi, R.L., Martin, D.S. and Fugman, R.A., 1971, "Spontaneous murine mammary adenocarcinoma: Model system for the evaluation of combined methods of therapy," Cancer Chemother. Rep. Part 1, 55:239. [Exhibit 83]
85. Stolfi, R.L., Stolfi, L.M., Sawyer, R.C., and Martin, D.S., 1988, "Chemotherapeutic evaluation using clinical

Applicants : MARTIN et al.
U.S. Serial No.: 10/518,003
Filed : March 14, 2005
Examiner : Lawrence E. Crane
Page : 16

Atty. Dkt. No. : 636-C-PCT-US
Art Unit : 1623
Date of SIDS : October 29, 2007

criteria in spontaneous, autochthonous murine breast tumors," J. Nat. Cancer Inst., 80:52-5. **[Exhibit 84]**

86. Street, J.C., Mahmoud, V., Ballon, D., Alfieri, A.A., and Koutcher, J.A., 1996, "13C and 31p NMR investigation of effect of 6-aminonicotinamide on metabolism of RIF-1 tumor cells in vitro," J. Biol. Chem., 271:4113-4119. **[Exhibit 85]**

87. Street, J.C., Alfieri, A.A., and Koutcher, J.A., 1997, "Quantitation of metabolic and radiobiological effects of 6-aminonicotinamide in RIF-1 tumor cells in vitro," Cancer Res., 57:3956-3962. **[Exhibit 86]**

88. Susin, S.A., Zamzami, N., Castedo, M., Hirsch, T., Marchetti, P., Macho, A., Dauges, E., Gauskens, M. and Kroemer, G., 1996, "Bcl-2 inhibits the mitochondrial release of an apoptogenic protease," J. Exp. Med., 184:1331-1342. **[Exhibit 87]**

89. Tanizawa, A., Kubota, M., Hashimoto, H., Shimizu, T., Takimoto, T., Kitoh, T., Akiyama, Y., and Mikama, H., 1989, "VP-16-induced nucleotide pool changes and poly (ADP-ribose) synthesis: The role of VP-16 in interphase death," Exp. Cell Res., 185:237-246. **[Exhibit 88]**

90. Tian, W-N., Braunstein, L.D., Apse, K., Pang, J., Rose, M, Tian, X. and Stanton, R.C., 1998, "Importance of Glucose-6-phosphate dehydrogenase activity for cell growth," J. Biol. Chem., 273:10609-10617. **[Exhibit 89]**

Applicants : MARTIN et al.
U.S. Serial No.: 10/518,003
Filed : March 14, 2005
Examiner : Lawrence E. Crane
Page : 17

Atty. Dkt. No. : 636-C-PCT-US
Art Unit : 1623
Date of SIDS : October 29, 2007

91. Tian, W-N., Braunstein, L.D., Apse, K., Pang, J., Rose, M., Tian, X., and Stanton, R.C., 1999, "Importance of glucose-6-phosphate dehydrogenase activity in cell death," Am. J. Physiol., 276 (Cell Physiol. 45):C1121-C1131. **[Exhibit 90]**
92. Tyagi, A.K. and Cooney, D.A., 1984, "Biomedical pharmacology, metabolism and mechanism of action of L-alanosine, a novel, natural antitumor agent," Adv. Pharmacal. Chemother. 20:69-121. **[Exhibit 91]**
93. Warnick, C.T., and Patterson, A.R.P., 1973, "Effect of methylthioinosine on nucleoside concentration in L5158 cells," Cancer Res., 33:1711-1715. **[Exhibit 92]**
94. Wielinga, P.R., Reid, G., Challa, E.E., van der Heijden, I., van Deemter, L., De Haas, M., Mol, C., Kuil, A.J., Groeneveld, E., Schuetz, J.D., Brouwer, C., De Abreu, R.A., Wijnholds, J., Beijnen, J.H. and Borst, P., 2002, "Thiopurine metabolism and identification of the Thiopurine metabolites transported by MRP4 and MRP5 overexpressed in human embryonic kidney cells," Mol. Pharm., 62:1321-1331. **[Exhibit 93]**
95. Williams-Ashman, H.G., Seidenfeld, J. and Galletti, P., 1982, "Trends in the biochemical pharmacology of 5'-deoxy-5'-methylthioadenosine," Biochem. Pharmacol., 31:277-288. **[Exhibit 94]**
96. Woods, R.A., Henderson, R.M., and Henderson, J.F., 1978, "Consequences of inhibition of purine biosynthesis de novo by 6-methylmercaptapurine ribonucleoside in

Applicants : MARTIN et al.
U.S. Serial No.: 10/518,003
Filed : March 14, 2005
Examiner : Lawrence E. Crane
Page : 18

Atty. Dkt. No. : 636-C-PCT-US
Art Unit : 1623
Date of SIDS : October 29, 2007

cultured lymphoma L5178 cells," Euro. J. Cancer, 14:765-70. **[Exhibit 95]**

97. Wyllie, A.H., 1993, "Apoptosis [The 1992 Frank Rose Memorial Lecture]," Br. J. Cancer., 67:205-208. **[Exhibit 96]**

98. Xiang, J., Chao, T. and Korsmyer, S.J., 1996, "Bax-induced cell death may not require interleukin 1-converting enzyme-like proteases," Proc. Natl. Acad. Sci. USA, 93:14359-14563. **[Exhibit 97]**

99. Yoshida, H., Kong, Y.Y., Yoshida, R., Elia, A.J., Hakem, R., Penninger, J.M. and Mak, T.W., 1998, "Apaf-1 is required for mitochondrial pathways of apoptosis and brain development," Cell, 94:739-750. **[Exhibit 98]**

100. Young, I., Young, G.L., Wiley, J.S. and van der Weyden, M.B., 1985, "Nucleoside transport and cytosine arabinoside (ara C) metabolism in human T lymphoblasts resistant to ara C, thymidine and 6-methymercaptopurine riboside," Eur. J. Cancer Clin. Oncol., 21(9):1077-1082. **[Exhibit 99]**

101. Zamzami, N., Susin, S.A., Marchetti, P., Hirsch, T., Gomez-Monterrey, I., Castedo, M., and Kroemer, G., 1996, "Mitochondrial control of nuclear apoptosis (see contents)," J. Exp. Med., 183:1533-44. **[Exhibit 100]**

102. Zou, H., Li, Y., Liu, X., and Wang, X., 1999, "An apaf-1-cytochrome c multimeric complex is a functional

Applicants : MARTIN et al.
U.S. Serial No.: 10/518,003
Filed : March 14, 2005
Examiner : Lawrence E. Crane
Page : 19

Atty. Dkt. No. : 636-C-PCT-US
Art Unit : 1623
Date of SIDS : October 29, 2007

apoptosome that activates procaspase-9," J. Biol. Chem.,
274:11549-11556. **[Exhibit 101]**

103. European Communication for SLOAN-KETTERING INSTITUTE
FOR CANCER RESEARCH, European Application No. 01986104.6
(Atty. Dkt. #636-A-PCT-EPO), Filed July 2, 2003, Dated
September 6, 2007. **[Exhibit 102]**

104. U.S. Office Action for MARTIN et al., U.S. Serial No.
10/172,346 (Atty. Dkt. #636-B), Filed June 13, 2002,
Dated November 19, 2003. **[Exhibit 103]**

105. U.S. Office Action for MARTIN et al., U.S. Serial No.
10/172,346 (Atty. Dkt. #636-B), Filed June 13, 2002,
Dated June 15, 2005. **[Exhibit 104]**

106. U.S. Office Action for MARTIN et al., U.S. Serial No.
10/172,346 (Atty. Dkt. #636-B), Filed June 13, 2002,
Dated June 15, 2006. **[Exhibit 105]**

107. Notice of Allowance and Fee(s) Due and Notice of
Allowability, for MARTIN et al., U.S. Serial No.
10/172,346 (Atty. Dkt. #636-B), Filed June 13, 2002,
Dated August 20, 2007. **[Exhibit 106]**

108. NIH R01 Grant Information for 1R01CA098505-1A3, PI
Jason Koutcher, Project Title "Cytocidal Therapy In Vivo
for Drug-Resistant Tumors," previously submitted for
U.S. Serial No. 10/172,346 (Atty. Dkt. #636-B). **[Exhibit
107]**

Applicants : MARTIN et al.
U.S. Serial No.: 10/518,003
Filed : March 14, 2005
Examiner : Lawrence E. Crane
Page : 20

Atty. Dkt. No. : 636-C-PCT-US
Art Unit : 1623
Date of SIDS : October 29, 2007

109. National Cancer Institute RAID Grant Information, PI
Maiyer Rizvi, previously submitted for U.S. Serial No.
10/172,346 (Atty. Dkt. #636-B). **[Exhibit 108]**

Applicants : MARTIN et al.
U.S. Serial No.: 10/518,003
Filed : March 14, 2005
Examiner : Lawrence E. Crane
Page : 21

Atty. Dkt. No. : 636-C-PCT-US
Art Unit : 1623
Date of SIDS : October 29, 2007

If a telephone interview would be of assistance in advancing the prosecution of the subject application, Applicants' undersigned attorney invites the Examiner to telephone him at the number provided below. No fee is deemed necessary in connection with the filing of this Supplemental Information Disclosure Statement. However, if any fee is required, authorization is hereby given to charge the amount of any such fee to Deposit Account No. 50-1891.

Respectfully submitted,

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